

### **Remarks**

Claims 10-14 and 23-32 are pending in the instant application. Claims 10-14 and 23-32 stand rejected under 35 U.S.C. §102(b) as being anticipated by United States Patent No. 5,368,840 to Unger. Claims 10-12, 23-27, 29, and 31 stand rejected under 35 U.S.C. §102(b) as being anticipated by United States Patent No. 5,250,285 to Lauffer. Claims 10-14 and 23-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over either one of United States Patent No. 5,958,373 to Garrity or United States Patent No. 5,277,895 to Platzek in view of either one of Unger or Lauffer. Claims 30-32 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Unger or Lauffer in view of United States Patent No. 5,190,744 to Rocklage. The application has been amended. Specifically, claim 23 has been amended to incorporate the elements of claim 10. Additionally, new claims 33 and 34 have been added which combine subject matter from now-canceled claims 11 and 12, respectively. Applicants respectfully submit that none of the amendments constitute new matter in contravention of 35 U.S.C. §132. Reconsideration is respectfully requested.

Claims 10-14 and 23-32 stand rejected under 35 U.S.C. §102(b) as being anticipated by United States Patent No. 5,368,840 to Unger. This rejection is respectfully traversed.

The present invention provides a method for detecting regions with decreased vascular perfusion by administering a physiologically tolerable compounds of Eu(II) and particular chelates.

The Examiner cites Unger for disclosing the administration of an MRI contrast agent comprising a physiologically tolerable Eu(II) compound. The Examiner also states that these Eu(II) compounds may be complexed to targeting moieties such as polymers, antibodies, etc.

Applicants respectfully submit, however, that Unger does not in fact disclose Eu(II) compounds. Referring to the cited column 6, lines 30-65, it is seen that among the compounds cited are Eu(III) and Er(II). Thus, Unger actually discloses an erbium compound, Er(II), and not the europium compound, Eu(II), of the present invention. Moreover, Eu(II) is not disclosed by Unger.

Therefore, as Unger fails to disclose, teach, or suggest imaging using Eu(II) compounds as is presently claimed, Unger fails to render the present invention unpatentable. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 10-12, 23-27, 29, and 31 stand rejected under 35 U.S.C. §102(b) as being anticipated by United States Patent No. 5,250,285 to Lauffer. This rejection is respectfully traversed.

Lauffer discloses hydroxy-aryl substituted chelates. The hydroxy-aryl groups increase the lipophilicity and hydrophobicity of the chelates and thus of the imaging

agent consisting of a metal ion and said chelates. Lauffer states that the hydroxy-aryl groups are necessary for his compounds to work as blood pool imaging agents (see e.g., col. 1, lines 31-64).

Applicants' claim 23, as amended, and new claims 33 and 34 do not include hydroxy-aryl groups. The compounds employed by the present invention are therefore hydrophilic and not – as the Lauffer chelates – lipophilic. Applicants respectfully submit that Lauffer therefore teaches away from the present invention, namely the use of hydrophilic Eu(II) complexes for the NMR imaging of regions with decreased vascular perfusion, i.e. for blood pool imaging.

The Examiner states that Lauffer discloses the chelates as presently claimed by claims 10 and 11, e.g. DOTA (Lauffer col. 13, l. 50+). However, upon closer examination, Lauffer states “.....In contrast, the ligand DOTA, which is a known chelate, lacks hydrophobic substituents and as such is unsuitable for NMR image enhancement of the liver and the blood pool”. Clearly Lauffer is teaching away from the present invention.

Additionally, new claim 33 (which incorporates the limitations of now-canceled claim 11), specifically disclaims hydroxy-aryl groups. As such, Applicants respectfully submit that Lauffer fails to disclose, teach, or suggest the claimed invention.

Similarly, new claim 34 incorporates the limitations of now-canceled claim 12, however it does not claim aryls in the definition of R2 (all other groups R, R1 and R3 are already hydrophilic groups) and from the definition of R4, R5 and R6 in formula (VI). Therefore, Applicants respectfully submit that Lauffer fails to disclose, teach or suggest the claimed invention.

As Lauffer fails to disclose, teach, or suggest the present invention, Applicants respectfully submit that the present invention is therefore patentably distinct thereover. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 10-14 and 23-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over either one of United States Patent No. 5,958,373 to Garrity or United States Patent No. 5,277,895 to Platzek in view of either one of Unger or Lauffer. This rejection is respectfully traversed.

As the Examiner states, Garrity and Platzek teach the use of Eu-complexes but fail to disclose that Eu is specifically Eu(II). As shown hereinabove, Unger also fails to teach Eu(II). Thus, Applicants respectfully submit that there is nothing in Unger which will correct the deficiencies of Garrity and Platzek. As such, the present invention is patentably distinct from the cited combination of Garrity, Platzek, and Unger.

Additionally, Lauffer regards Eu(II) being equivalent to other paramagnetic metal ions known in the art, but, as also described above, teaches away from combining it with

the "normal" chelating agents disclosed by Garrity and Platzek as is presently claimed. Therefore, Applicants respectfully submit that as Laufer teaches away from correcting the deficiencies of the Garrity and Platzek, the present application is patentably distinct thereover.

As neither the combination of Garrity and Platzek with either of Unger or Laufer renders the present invention unpatentable, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 30-32 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Unger or Laufer in view of United States Patent No. 5,190,744 to Rocklage. This rejection is respectfully traversed.

Rocklage is cited for disclosing imaging of blood perfusion and the like. However, as Unger does not disclose Eu(II) and as Laufer teaches away from using Eu(II) complexes comprising the chelates incorporated from now-canceled claims 10, 11 and 12, Applicants submit that the combination of both teachings with Rocklage would still not have lead to the present invention. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the amendments and remarks hereinabove, Applicants respectfully submit that the instant application, including claims 13-14 and 23-34 are in condition for allowance. Favorable action thereon is respectfully requested.

The Office is hereby authorized to charge any fees be incurred by the entry of this amendment to deposit account no. 502-665 of the assignee of the present invention.

Should the Examiner have any questions with respect to the foregoing, he is respectfully invited to contact Applicant's undersigned counsel at the telephone number below.

Respectfully submitted,



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